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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/888,126	06/22/2001	Jennifer L. Schmitke	2685.2030-000	9053

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EXAMINER	
HAGHIGHATIAN, MINA	

ART UNIT	PAPER NUMBER
1616	

DATE MAILED: 08/11/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/888,126	SCHMITKE ET AL.	
	Examiner	Art Unit	
	Mina Haghighatian	1616	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on *22 April 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3-18,20-39 and 41-60* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1, 3-18, 20-39, 41-60* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Receipt is acknowledged of Applicant's Response, Amendments and Declaration filed on 04/22/04. Claims 2, 29 and 40 were cancelled and no new claims were added.

Claim Rejections - 35 USC § 103

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claims 1, 3-18, 20-39 and 41-60 are rejected under 35 U.S.C. 103(a) as being unpatentable over Patton et al (5,997,848) in view of Edwards et al (5,985,309).

Patton teaches that systemic delivery of insulin to a mammalian host is accomplished by inhalation of a dry powder of insulin, which is rapidly absorbed through the alveolar regions of the lung. Insulin dry powders are prepared by dissolving insulin in an aqueous buffer to form a solution and spray drying the solution to produce substantially amorphous particles having a particle size less than 10 micron, preferably less than in the range of 0.1 to 5 micron. Optionally the pharmaceutical carrier is also dissolved in the buffer, to form a homogenous solution, wherein spray drying of the solution produces individual particles comprising insulin, carrier buffer and any other compounds which were present in the solution. The carrier is preferably an amino acid, such as glycine, lysine, etc (col. 3, lines 9-21; 53-68 and col. 4, lines 43-60).

Patton discloses that insulin dry powders suitable for use in the present invention include amorphous insulin, crystalline insulin or mixtures thereof. The preferred method

of forming insulin powders comprising particulates in the desired size range is spray drying, where pure bulk insulin is first dissolved in a physiologically acceptable aqueous buffer, typically a citrate buffer such as sodium citrate (col. 6, lines 11-16 and 43-67). The preferable concentration ranges for insulin is 5 to 95%, preferably from 20 to 80% and for the carrier material is 5 to 95%. The presence of carrier material in the particles which are delivered to the alveolar region of the lung has been found not to significantly interfere with systemic absorption of insulin (col. 7, lines 1-27).

Patton also discloses that the individual dosages on a per inhalation basis, typically being in the range from 0.5 mg to 10 mg, and the total dosage during a single respiratory administration is in the range of 0.5 to 15 mg (col. 8, lines 25-32). Patton, while teaching amino acids as carriers, lacks disclosure on DPPC.

Edwards teaches particle incorporating a surfactant and/or a hydrophilic or hydrophobic complex of a positively or negatively charged therapeutic agent and a charged molecule of opposite charge for drug delivery to the pulmonary system, methods of preparation and administration. Exemplary surfactants include dipalmitoylphosphatidylcholine (DPPC). Exemplary hydrophilic or hydrophobic complexes include insulin and protamine. The particles are aerodynamically light particles with a tap density of less than 0.4 g/cm^3, a mean diameter between 5 and 30 micron and an aerodynamic diameter between 1 and 5 microns (col. 3, line 56 to col. 4, line 17).

Edwards discloses that administration of the particles to the lung by aerosolization permits deep lung delivery of relatively large diameter therapeutic aerosols, for example greater than 5 micron in mean diameter. The particles can be fabricated with features which enhance aerosolization via dry powder inhaler devices, and lead to lower deposition in the mouth, throat and inhaler device (col. 5, lines 29-47).

Edwards also discloses that in addition to the therapeutic agents, the formulations may and preferably do include one or more excipients such as sugars, proteins and surfactant (col. 6, line 65 to col. 7, line 2). Targeting molecules can be attached to the particles via reactive functional groups on the particles. For example, targeting molecules can be attached to the amino acid groups of functionalized polyester graft copolymer particles such as poly(lactic acid-co-lysine) (col. 11, lines 48-60). Therapeutic agents suitable for such preparation include insulin (col. 12, lines 16-47).

Edwards discloses examples of particles such as insulin:albumin:lactose:DPPC in example 9. The particles are said to comprise 60% DPPC, 2% insulin, 19% albumin and 19% lactose. Two solutions are made of the ingredients, then they are combined and spray dried to produce particles. Example 11 discloses preparation method of sustained release insulin particles and example 12 discloses preparation of insulin:protamin:zinc complexes.

It would have been obvious to a person of ordinary skill in the art at the time the invention was made to have modified the formulations of Patton containing insulin,

buffers and carriers with insulin formulations and method of delivering the insulin formulations to the lung as taught by Edwards and to have implemented DPPC as the carrier, since it was disclosed that DPPC is an exemplary surfactant, naturally occurring in the lung.

Double Patenting

Claims 1, 3-18, 20-39 and 41-60 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims of copending Application No. 10/ 179,463 in view of Patton et al (5,997,848). Although the conflicting claims are not identical, they are not patentably distinct from each other because the examined claims would have been obvious over the reference claims. Specifically claim 1 of the instant application recites a formulation containing approximately 60% DPPC, approximately 30% insulin and approximately 10% sodium citrate. The claims of the copending application No. 10/179,463 recite the same formulation with a difference in concentration ranges of DPPC and insulin (75% and 15% respectively). Patton et al discloses formulations where the amount of insulin can be from 5 to 95% and preferably 20 to 80%. Thus it would have been obvious to one of ordinary skill in the art to have modified the concentration ranges of insulin so that various dosage would be available to patients. Also in dependent claims the variation of concentration ranges for DPPC is an optimization of ranges and would vary according to the amount of active agent desired for the preparation.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Response to Arguments

Applicant's arguments, filed 04/22/04, with respect to the rejection(s)of claim(s) 1-60 have been fully considered and are persuasive. Therefore, the rejection has been withdrawn. However, upon further consideration, a new ground(s) of rejection is made.

Applicant's Declaration has been fully considered, but found not persuasive, especially in light of the new rejection. Declaration primarily shows that formulations containing 10% insulin were not stable, where formulations containing 30% insulin appear to perform better and show sufficient stability. However the primary reference in the new rejection, Patton et al, discloses formulations containing from 5 to 95% and preferably from 20 to 80% insulin.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Mina Haghighatian whose telephone number is 571-272-0615. The examiner can normally be reached on core office hours.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary L. Kunz can be reached on 571-272-0887. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

MH

Mina Haghighatian
August 06, 2004

MICHAEL G. HARTLEY
PRIMARY EXAMINER